

血液・膠原病・感染症内科学講座

【研究プロジェクト名および概要】

- I. ヒトT細胞白血病ウイルス1型の発がん機構
- II. 成人T細胞白血病(ATL)の臨床、病態解析と治療開発
- III. 白血病の発症機構の解析に基づく病態研究と新しい治療法の開発
- IV. 悪性リンパ腫、骨髄腫および原発性アミロイドーシスの病態解析と新規治療法開発へ向けたトランスレーショナルリサーチ
- V. 膜原病・自己免疫疾患の病態解析と治療
- VI. 後天性免疫不全症候群(AIDS)の病態解析とその分子標的治療剤開発へ向けたトランスレーショナルリサーチ
- VII. 発作性夜間ヘモグロビン尿症(PNH)や慢性骨髄白血病(CML)などの造血幹細胞疾患の臨床及び基礎研究
- VIII. 血液凝固系の臨床及び基礎研究

【教職員および大学院学生】

准教授	安永 純一朗	I, II
助 教	河野 和	IV
助 教	七條 敬文	I, II, III, IV
大学院(博士課程)	上野 満徳	I, II, III, IV
大学院(博士課程)	園田 未祐	I, II, III, IV
大学院(博士課程)	IDRISS OSAMA MOHAMMED ALI HUSSEIN	I, II
大学院(博士課程)	張 文怡	I, II
大学院(博士課程)	奥村 真由	VI
大学院(博士課程)	ALI AHMED TARIG SALAH	I, II
大学院(修士課程)	白 俊哲	I, II
大学院(修士課程)	岡本 祐毅	I, II
大学院(修士課程)	坂田 亮	I, II
技術補佐員	松本 美穂	I, II
技術補佐員	西銘 由美	I, II

【研究プロジェクト】

【連絡先】電話：096-373-5156 FAX：096-373-5158

【ホームページ】<https://2naika.jp/>

【特殊技術・特殊装置】

- 1. P3 施設
- 2. Flow cytometer (FACSVerso, FACSLyric)
- 3. Confocal microscope
- 4. Next-generation sequencer (Illumina MiSeq)
- 5. Cell sorter (SONY SH800S)

【英文原著】

1. Toyoda K, Yasunaga JI, Shichijo T, Arima Y, Tsujita K, Tanaka A, Salah T, Zhang W, Hussein O, Sonoda M, Watanabe M, Kurita D, Nakashima K, Yamada K, Miyoshi H, Ohshima K and Matsuoka M. HTLV-1 bZIP factor-induced reprogramming of lactate metabolism and epigenetic status promote leukemic cell expansion. *Blood Cancer Discovery*. 2023 (In press).
2. N Sakurada-Aono M, Sakamoto T, Kobayashi M, Takiuchi Y, Iwai F, Tada K, Sasanuma H, Hirabayashi S, Murakawa Y, Shirakawa K, Sakamoto C, Shindo K, Yasunaga JI, Matsuoka M, Pommier Y, Takeda S, Takaori-Kondo A. HTLV-1 bZIP factor impairs DNA mismatch repair system. *Biochem Biophys Res Commun*. 2023 Mar 21;657:43-49. Doi: 10.1016/j.bbrc.2023.03.049.
3. Kameda T, Kataoka K, Kamiunten A, Hidaka M, Miyoshi H, Nakano N, Nosaka K, Yoshimitsu M, Yasunaga JI, Kogure Y, Shide K, Miyahara M, Sakamoto T, Akizuki K, Hidaka T, Kubuki Y, Koya J, Kawano N, Yamashita K, Kawano H, Toyama T, Maeda K, Marutsuka K, Imaizumi Y, Kato K, Sugio T, Tokunaga M, Tashiro Y,

- Takaori-Kondo A, Miyazaki Y, Akashi K, Ishitsuka K, Matsuoka M, Ohshima K, Watanabe T, Kitanaka A, Utsunomiya A, Ogawa S, Shimoda K. Integrated genetic and clinical prognostic factors for aggressive adult T-cell leukemia/lymphoma. *Haematologica*. 2023 Feb 16. doi: 10.3324/haematol.2022.281510. PMID: 36794502.
4. Yasunaga JI. Viral, genetic, and immune factors in the oncogenesis of adult T-cell leukemia/lymphoma. *Int J Hematol*. 2023 Jan 27. doi: 10.1007/s12185-023-03547-5. Online ahead of print. PMID: 36705848.
 5. Fuji S, Yasunaga JI, Watanabe E, Matsuoka M, Uchimaru K, Ishikawa J. Pseudo-progression of adult T-cell leukemia-lymphoma after cord blood transplantation. *Haematologica*. 2022. doi: 10.3324/haematol.2022.281175. Online ahead of print. PMID: 35734929.
 6. Shichijo T, Nosaka K, Tatetsu H, Higuchi Y, Endo S, Inoue Y, Toyoda K, Kikukawa Y, Kawakita T, Yasunaga JI, Matsuoka M. Beneficial impact of first-line mogamulizumab-containing chemotherapy in adult T-cell leukaemia-lymphoma. *Br J Haematol*, 2022. doi: 10.1111/bjh.18281. Online ahead of print. PMID: 35607839.
 7. Shichijo T, Tatetsu H, Nosaka K, Higuchi Y, Kikukawa Y, Inoue Y, Toyoda K, Yasunaga JI, Matsuoka M. Predictive impact of soluble interleukin-2 receptor and number of extranodal sites for identification of patients at very high risk of CNS relapse in diffuse large B-cell lymphoma. *EJHaem*, 3(2):385-393, 2022. doi: 10.1002/jha2.393.
 8. Hiyoshi M, Takahashi N, Eltalkhawy YM, Noyori O, Lotfi S, Panaampon J, Okada S, Tanaka Y, Ueno T, Fujisawa JI, Sato Y, Suzuki T, Hasegawa H, Tokunaga M, Satou Y, Yasunaga JI, Matsuoka M, Utsunomiya A, Suzu S. M-Sec induced by HTLV-1 mediates an efficient viral transmission. *PLoS Pathog*, 17(11):e1010126, 2022. doi: 10.1371/journal.ppat.1010126.
 9. Kogure Y, Kameda T, Koya J, Yoshimitsu M, Nosaka K, Yasunaga JI, Imaizumi Y, Watanabe M, Saito Y, Ito Y, McClure MB, Tabata M, Shingaki S, Yoshifuji K, Chiba K, Okada A, Kakiuchi N, Nannya Y, Kamiunten A, Tahira Y, Akizuki K, Sekine M, Shide K, Hidaka T, Kubuki Y, Kitanaka A, Hidaka M, Nakano N, Utsunomiya A, Sica RA, Acuna-Villaorduna A, Janakiram M, Shah UA, Ramos JC, Shibata T, Takeuchi K, Takaori-Kondo A, Miyazaki Y, Matsuoka M, Ishitsuka K, Shiraishi Y, Miyano S, Ogawa S, Ye BH, Shimoda K, Kataoka K. Whole-genome landscape of adult T-cell leukemia/lymphoma. *Blood*, 139(7):967-982, 2022. doi: 10.1182/blood.2021013568.
 10. Ono T, Takahashi N, Kizaki M, Kawaguchi T, Suzuki R, Yamamoto K, Ohnishi K, Naoe T, Matsumura I. Clinical outcomes of second-generation tyrosine kinase inhibitors versus imatinib in older patients with CML. *Cancer Sci* 114(3):995-1006, 2023.
 11. Nishiyama-Fujita Y, Nakazato T, Iriyama N, Tokuhira M, Ishikawa M, Sato E, Takaku T, Sugimoto K, Fujita H, Fujioka I, Tsuchiya S, Kimura Y, Iwanaga E, Komatsu N, Asou N, Kizaki M, Hatta Y, Kawaguchi T. Outcomes of adolescents and young adults with chronic-phase chronic myeloid leukaemia treated with tyrosine kinase inhibitors. *Ann Med* 54(1): 1244-1254, 2022.
 12. Ikezoe T, Noji H, Ueda Y, Kanda Y, Okamoto S, Usuki K, Matsuda T, Akiyama H, Shimono A, Yonemura Y, Kawaguchi T, Chiba S, Kanakura Y, Nishimura JI, Ninomiya H, Obara N. Long-term follow-up of patients with paroxysmal nocturnal hemoglobinuria treated with eculizumab: post-marketing surveillance in Japan. *Int J Hematol*. 115(4): 470-480, 2022.
 13. Fukuta T, Tanaka T, Hashimoto T, Isahaya K, Kubo Y, Yamano Y, Satomi K, Hiraoka N, Shirakawa N, Arakawa A, Ogawa C, Nishimura N, Aoki J, Ito A, Inamoto Y, Kim SW, Fukuda T. Nelarabine-induced myelopathy in patients undergoing allogeneic hematopoietic cell transplantation: a report of three cases. *Int J Hematol*. 2023 Jan 27. doi: 10.1007/s12185-023-03539-5. Epub ahead of print. PMID: 36705847.
 14. Kawano Y, Hata H, Takashio S, Tsujita K, Ueda M, Matsuoka M. Daratumumab, lenalidomide and dexamethasone in newly diagnosed systemic light chain amyloidosis patients associated with multiple myeloma. *Br J Haematol* 198(3): e38–e41, 2022.

15. Masuda T, Inamori Y, Furukawa A, Yamahiro M, Momosaki K, Chang CH, Kobayashi D, Ohguchi H, Kawano Y, Ito S, Araki N, Ong SE, Ohtsuki S. Water droplet-in-oil digestion method for single-cell proteomics. *Anal Chem* 94(29):10329-10336, 2022.
16. Kim K, Min CK, Koh Y, Ishizawa K, Kim SH, Ito S, Tanaka J, Uchiyama M, Kawano Y, Kim JS, Moreau P, Martin T, Dong Y, Risso ML, Suzuki K. Isatuximab plus carfilzomib and dexamethasone in East Asian patients with relapsed multiple myeloma: IKEMA subgroup analysis. *Int J Hematol* 116(4):553-562, 2022.
17. Tokai T, Takashio S, Kawano Y, Kidoh M, Oda S, Matsuoka M, Tsujita K. Assessing the treatment effect of daratumumab by serial measurements of cardiac biomarkers and imaging parameters in light-chain cardiac amyloidosis. *J Cardiol Cases* 26(4):301-304, 2022.
18. Ishida T, Ito S, Tanaka J, Uchiyama M, Kawano Y, Moreau P, Martin T, Risso ML, Tada K, Suzuki K, Ishizawa K. Isatuximab plus carfilzomib and dexamethasone in Japanese patients with relapsed multiple myeloma: subgroup analysis of the randomised, open label, phase 3 IKEMA study. *Jpn J Clin Oncol* 52(12):1446-1449, 2022.
19. Kawano Y, Matsuoka M. Difference in Clinical Assessments of Multiple Myeloma by Immunofixation Electrophoresis Systems. *International Journal of Myeloma* 13(1): 1-5, 2023.
20. Kidoh M, Oda S, Takashio S, Hirakawa K, Kawano Y, Shiraishi S, Hayashi H, Nakaura T, Nagayama Y, Funama Y, Ueda M, Tsujita K, Hirai T. CT extracellular volume fraction versus myocardium-to-lumen signal ratio for cardiac amyloidosis. *Radiology* 306(3): e220542, 2023.
21. Sacco A, Desantis V, Celay J, Giustini V, Rigali F, Savino FD, Cea M, Soncini D, Cagnetta A, Solimando AG, D'Aliberti D, Spinelli S, Ramazzotti D, Almici C, Todoerti K, Neri A, Anastasia A, Tucci A, Motta M, Chiarini M, Kawano Y, Martinez-Climent JA, Piazza R, Roccaro AM. Targeting the immune microenvironment in Waldenström Macroglobulinemia via halting the CD40/CD40-ligand axis. *Blood* 2023 (In Press)
22. Uchiba M, Matsuoka M. Using weighted harmonic mean for prediction of APTT in the mixing test. *Thrombosis Update* 8;100114,2022.
23. Hiramatsu H, Nosaka K, Kusumoto S, Nakano N, Choi I, Yoshimitsu M, Imaizumi Y, Hidaka M, Sasaki H, Makiyama J, Ohsuka E, Jo T, Ogata M, Ito A, Yonekura K, Tatetsu H, Kato T, Kawakita T, Suehiro Y, Ishitsuka K, Iida S, Matsutani T, Nishikawa H, Utsunomiya A, Ueda R, Ishida T. Landscape of immunoglobulin heavy chain γ gene class switch recombination in patients with adult T-cell leukemia-lymphoma. *Haematologica*. 2023 Apr 1;108(4):1173-1178.
24. Sekiguchi N, Rai S, Munakata W, Suzuki K, Handa H, Shibayama H, Endo T, Terui Y, Iwaki N, Fukuhara N, Tatetsu H, Iida S, Ishikawa T, Iguchi D, Izutsu K. Two-year outcomes of tirabrutinib monotherapy in Waldenström's macroglobulinemia. *Cancer Sci*. 2022 Jun;113(6):2085-2096.
25. Imaizumi Y, Iwanaga M, Nosaka K, Ishitsuka K, Ishizawa K, Amano M, Ishida T, Uike N, Utsunomiya A, Ohshima K, Tanaka J, Tokura Y, Tobinai K, Watanabe T, Uchimaru K, Tsukasaki K. Validation of the iATL-PI prognostic index in therapeutic decision-making for patients with smoldering and chronic ATL: a multicenter study. *Int J Hematol*. 117: 206-215, 2023.
26. Izutsu K, Makita S, Nosaka K, Yoshimitsu M, Utsunomiya A, Kusumoto S, Morishima S, Tsukasaki K, Kawamata T, Ono T, Rai S, Katsuya H, Ishikawa J, Yamada H, Kato K, Tachibana M, Kakurai Y, Adachi Y, Tobinai K, Yonekura K, Ishitsuka K. An Open-Label, Single-Arm, Phase 2 Trial of Valemetostat in Relapsed or Refractory Adult T-Cell Leukemia/Lymphoma. *Blood* 141: 1159-1168, 2023.
27. Morioka H, Ohge H, Nagao M, Kato H, Kokado R, Yamada K, Yamada T, Shimono N, Nukui Y, Yoshihara S, Sakamaki I, Nosaka K, Kubo Y, Kawamura H, Fujikura Y, Kitaura T, Sunakawa M, Yagi T; Research Group of Japan Infection Prevention and Control Conference for National and Public University Hospitals. Appropriateness of

- surgical antimicrobial prophylaxis in Japanese university hospitals. *J Hosp Infect* 129: 189-197, 2022.
- 28. Matsuo M, Ueno T, Monde K, Sugata K, Tan BJJ, Rahman A, Miyazato P, Uchiyama K, Islam S, Katsuya H, Nakajima S, Tokunaga M, Nosaka K, Hata H, Utsunomiya A, Fujisawa JI, Satou Y. Identification and characterization of a novel enhancer in the HTLV-1 proviral genome. *Nat Commun.* 13: 2405, 2022.
 - 29. Yano H, Fujiwara Y, Horlad H, Pan C, Kai K, Niino D, Ohsawa K, Higashi M, Nosaka K, Okuno Y, Tamaru JI, Mukasa A, Matsuoka M, Komohara Y. Blocking cholesterol efflux mechanism is a potential target for antilymphoma therapy. *Cancer Sci* 113: 2129-2143, 2022.
 - 30. Tanaka N, Mori S, Kiyotani K, Ota Y, Gotoh O, Kusumoto S, Nakano N, Suehiro Y, Ito A, Choi I, Ohtsuka E, Hidaka M, Nosaka K, Yoshimitsu M, Imaizumi Y, Iida S, Utsunomiya A, Noda T, Nishikawa H, Ueda R, Ishida T. Genomic determinants impacting the clinical outcome of mogamulizumab treatment for adult T-cell leukemia/lymphoma. *Haematologica* 107: 2418-2431, 2022.
 - 31. Matsumoto K, Kuwata T, Tolbert WD, Richard J, Ding S, Prévost J, Takahama S, Judicate GP, Ueno T, Nakata H, Kobayakawa T, Tsuji K, Tamamura H, Smith AB 3rd, Pazgier M, Finzi A, Matsushita S. Characterization of a Novel CD4 Mimetic Compound YIR-821 against HIV-1 Clinical Isolates. *J Virol.*;97(1):e0163822. (2023) doi: 10.1128/jvi.01638-22. PMID: 36511698.
 - 32. Nagayoshi Y, Nishiguchi K, Yamamura R, Chujo T, Oshima H, Nagata H, Kaneko H, Yamamoto K, Nakata H, Sakakida K, Kunisawa A, Adachi M, Kakizoe Y, Mizobe T, Kuratsu JI, Shimada S, Nakamori Y, Matsuoka M, Mukoyama M, Wei FY, Tomizawa K. t6A and ms2t6A Modified Nucleosides in Serum and Urine as Strong Candidate Biomarkers of COVID-19 Infection and Severity. *Biomolecules*;12(9):1233. (2022) doi: 10.3390/biom12091233. PMID: 36139072.
 - 33. Oka K, Matsumoto A, Tetsuka N, Morioka H, Iguchi M, Ishiguro N, Nagamori T, Takahashi S, Saito N, Tokuda K, Igari H, Fujikura Y, Kato H, Kanai S, Kusama F, Iwasaki H, Furuhashi K, Baba H, Nagao M, Nakanishi M, Kasahara K, Kakeya H, Chikumi H, Ohge H, Azuma M, Tauchi H, Shimono N, Hamada Y, Takajo I, Nakata H, Kawamura H, Fujita J; Japan Infection Prevention and Control Conference for National and Public University Hospitals. Clinical characteristics and treatment outcomes of carbapenem-resistant Enterobacteriales infections in Japan. *J Glob Antimicrob Resist.*: 29:247-252. (2022) doi: 10.1016/j.jgar.2022.04.004. PMID: 35429667.
 - 34. Katsuya H, Cook LBM, Rowan AG, Melamed A, Turpin J, Ito J, Islam S, Miyazato P, Jek Yang Tan B, Matsuo M, Miyakawa T, Nakata H, Matsushita S, Taylor GP, Bangham CRM, Kimura S, Satou Y. Clonality of HIV-1- and HTLV-1-Infected Cells in Naturally Coinfected Individuals. *J Infect Dis.* 225(2):317-326. (2022) doi: 10.1093/infdis/jiab202.
 - 35. Zhao T, Wang Z, Fang J, Cheng W, Zhang Y, Huang J, Xu L, Gou H, Zeng L, Jin Z, Matsuoka M. HTLV-1 activates YAP via NF-κB/p65 to promote oncogenesis. *Proc Natl Acad Sci U S A.* 2022 Mar 1;119(9):e2115316119. doi: 10.1073/pnas.2115316119.
 - 36. Matsuoka M. Targeting vulnerabilities of adult T-cell leukemia. *Blood.* 2022 Mar 10;139(10):1435. doi: 10.1182/blood.2021014879.
 - 37. Toyoda K, Matsuoka M. Functional and Pathogenic Roles of Retroviral Antisense Transcripts. *Front Immunol.* 2022 Apr 29;13:875211. doi: 10.3389/fimmu.2022.875211. eCollection 2022.
 - 38. Mizuhashi Y, Hirata S, Sakata K, Miyagawa E, Iwakura M, Murai M, Sasai T, Matsuoka M. Overlap syndrome involving anti-OJ antibody-positive polymyositis, systemic lupus erythematosus and Sjögren's syndrome: A case report and literature review. *Mod Rheumatol Case Rep.* 2022 Nov 25:rxac087. doi: 10.1093/mrcr/rxac087. Online ahead of print.

39. Kawano Y, Sasano T, Arima Y, Kushima S, Tsujita K, Matsuoka M, Hata H. A novel PDK1 inhibitor, JX06, inhibits glycolysis and induces apoptosis in multiple myeloma cells. *Biochem Biophys Res Commun.* 2022 Jan 8;587:153-159. doi: 10.1016/j.bbrc.2021.11.102.
40. Amano M, Otsu S, Maeda K, Uemura Y, Shimizu Y, Omata K, Matsuoka M, Shimada S, Mitsuya H. Neutralization activity of sera/IgG preparations from fully BNT162b2 vaccinated individuals against SARS-CoV-2 Alpha, Beta, Gamma, Delta, and Kappa variants. *Sci Rep.* 2022 Aug 8;12(1):13524. doi: 10.1038/s41598-022-17071-9.
41. Inoue Y, Nishimura N, Murai M, Matsumoto M, Watanabe M, Yamada A, Izaki M, Nosaka K, Matsuoka M. Prevention of acute graft-versus-host disease in adult T-cell leukemia-lymphoma patients who received mogamulizumab before allogeneic hematopoietic cell transplantation. *Int J Hematol.* 2022 Mar;115(3):435-439. doi: 10.1007/s12185-021-03250-3. Epub 2021 Oct 27.

【和文総説】

1. 平田真哉. 【膠原病・リウマチ診療における薬剤使用上の注意】タクロリムス, リウマチ科68(1):11-17, 2022年7月.
2. 河野和. 多発性骨髄腫におけるCD38標的療法の意義. 血液内科84(4):532-535, 2022.
3. 豊田康祐, 七條敬文. Risk stratification and therapeutic strategy for peripheral T-cell lymphoma. 血液内科. 84(6):822-828, 2022.
4. 七條敬文. Role of consolidative stem cell transplant in CD30+PTCL patients with CR following first-line treatment (a post-hoc subgroup analysis of the ECHELON-2 trial). 血液内科. 86(2):240-245, 2023.
5. 七條敬文. Lymphoma of testis(testicular lymphoma). 新リンパ腫学. 81(3):423-427, 2023.
6. 七條敬文, 松岡雅雄. Immunodeficiency caused by HTLV-1 infection and adult T-cell leukemia/lymphoma. 臨床免疫・アレルギー学. in press, 2023.
7. 内場光浩. がんとDIC(線溶異常を含めて). 日本検査血液学会雑誌 23(2):322-327, 2022.
8. 内場光浩. FDPとD-ダイマーの標準化の限界と臨床検査としての有用性. 日本検査血液学会雑誌 24(1):85-90, 2022.
9. 立津央, 今金大輔, 野坂生郷, 加留部謙之輔, 本田由美, 樋口悠介, 安永純一朗, 三上芳喜, 松岡雅雄. ステロイドが著効した濾胞性T細胞リンパ腫. 臨床血液2022年63巻11号p. 1497-1502